REMARKS

Claim 1-7 and 23-54 are pending. Claim 41 is rejected. Claims 8-22 are canceled by this communication. Claims 42-54 are newly added.

Objection to the specification

The Examiner objects to the specification. Applicant believes this objection is moot in light of the amendment to the specification.

Sequence Listing

The Examiner objected to the previously filed sequence listing. Applicant believes this objection is moot in view of the new sequence listing filed on April 27, 2007.

Rejection under 35 U.S.C. 112

Claim 41 is rejected under 35 U.S.C. 112, first paragraph, for allegedly lacking sufficient support. Applicant respectfully disagrees.

The Examiner alleges that the specification provides only a single sequence of NELL-1 nucleic acid. Applicant respectfully directs the Examiner's attention to page 8, paragraph [0027], where the specification provides NELL-1 cDNA and NELL-1 genomic DNA as described in Watanabe et al., Genomics 38(3):273-276 (1996); Ting et al., J. Bone Mineral. Res., 14:80-89 (1999); and GeneBank Accession Number U57523. At page 8, paragraph [0028], the specification defines the NELL-1 protein as one expressed by the NELL-1 gene or cDNA, which is readily acertainable by an ordinary artisan in the art. Therefore, the NELL-1 protein includes any protein expressed by the NELL-1 nucleic acid sequence described in the specification and other NELL-1 nucleic acid sequences, which were documented and known to an ordinary artisan. Further, paragraph [0028] defines the NELL-1 protein to include NELL-1 protein fragments that retain the ability to induce bone mineralization. It is settled law that "an adequate written

description of an invention that involves a biological macromolecule" does not have to include "recitation of known structure" of the macromolecule (see, MPEP §2163; see also Falkner v. Inglis, 448 F.3d 1357, 1366, 79 USPQ2d 1001, 1007 (Fed. Cir. 2006) (holding "the Board erred in holding that the specification do not meet the written description requirement because they do not reiterate the structure or formula or chemical name for the nucleotide sequences of the claimed chimeric genes" where the genes involved known DNA segments).

Accordingly, claim 41 has sufficient support in the specification under 35 U.S.C. 112, first paragraph.

Rejection under 35 U.S.C. 102

Claim 41 is rejected under 35 U.S.C. 102(b) as being anticipated by WO 01/24821 by Ting ("Ting"). Applicant respectfully disagrees.

Claim 41 defines a pharmaceutical formulation comprising: (a) one or more active agents in **an amount effective for increasing osteoblast differentiation** in a human being selected from a nucleic acid encoding a Nell-1 protein, a Nell-1 protein, and an agent that alters expression or activity of a Nell-1 protein; and (b) a pharmaceutically acceptable excipient.

Ting describes modulation of expression level of Nell-1 affects bone mineralization. **Ting does not describe a formulation as defined by claim 41, which is effective for osteoblast differentiation.** As an ordinary skill in the art would recognize, bone mineralization is a process in bone rebuilding that may reflect locally passive chemical processes, requiring only the presence of appropriate local concentrations of the precipitating ions. Bone mineralization is also influenced by local factors such as osteoclasts that resorb bone and non-local factors such as dietary intake and systemic levels of calcium and phosphate. In contrast, osteoblast differentiation is a process in bone generation that requires higher-order functions of

cells. As an example, etidronate is a anti-osteoporosis medication that causes chemical changes to the mineral itself, inhibiting crystal formation and making the mineral resistant to resorption and/or inhibiting osteoblast activity; however, it does not increase osteoblast differentiation (http://courses.washington.edu/bonephys/biseffects.html). Therefore, bone mineralization and osteoblast differentiation are two distinct processes in a bone tissue. A formulation effective for increasing or decreasing bone mineralization may not be effective for increasing or decreasing osteoblast differentiation, and vice versa.

In sum, claim 41 is patentably allowable over Ting under 35 U.S.C. 102(b). Claims 42-54 depend from claim 41 and are patentably allowable over Ting for at least the same reason.

CONCLUSION

Withdrawal of the rejection and allowance of the claims is respectfully requested. **If the Examiner has any suggestions or amendments to the claims to place the claims in condition for allowance, applicant would prefer a telephone call to the undersigned attorney for approval of an Examiner's amendment.** If the Examiner has any questions or concerns, the Examiner is invited to telephone the undersigned attorney at (415) 393-9885.

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